

050553235

HYPERTENSION PRAGUE 2002

134



19th Scientific Meeting of the
International Society of Hypertension
12th European Meeting on Hypertension
June 23 - 27, 2002 • Prague, Czech Republic

P0748 INFLUENCE OF TAMOXIFEN ON CAROTID INTIMA-MEDIA THICKNESS IN POSTMENOPAUSAL WOMEN

Simon D, Boulay P, Simon JM, Toumpanou C, Tropea O, Lalou B, Jallou P, Laurent S, Pharmacology Unit, Hôpital Pitié Salpêtrière, Paris, France; Cancerology Unit, Hôpital Pitié Salpêtrière, Paris, France. E-mail: pierre.boulayrie@ggk.ap-hop-paris.fr

Objective: Previous studies have suggested beneficial effects of selective estrogen receptor modulators (SERM) on cardiovascular risk factors in postmenopausal women. Increased thickness of the intima-media complex of the common carotid artery (IMT-CCA) is an early marker of atherosclerosis. Tamoxifen (T) is a mixed estrogen agonist/antagonist. SERM, with as yet unexplored effects on carotid artery structure. The goal of this case-control study was to determine the influence of tamoxifen on IMT-CCA in postmenopausal women.

Design and Methods: With a predefined calculation of number of patients (B-risk = 0.20): sixty seven postmenopausal women with breast cancer treated for more than one year with tamoxifen (20 mg/day) and 37 postmenopausal women with cancer never tamoxifen treated were enrolled in the study. IMT and internal diameter of the carotid artery were non-invasively determined with high-definition echotracking device performed in a central core laboratory blinded to the treatment. Pulse pressure (PP) was measured locally with applanation tonometry.

Results: Both groups were similar for demographic and clinical characteristics including cardiovascular risk factor. The mean duration of tamoxifen treatment was 2.4±0.9 years. IMT and internal diameter were significantly lower in tamoxifen group than in control group (609±147 µm vs 662±149 µm, p=0.04 and 4.89±0.60 mm vs 5.12±0.58 mm, p=0.03, respectively). Pulse pressure was not influenced by the use of tamoxifen. After adjustment for age, body surface area, smoking status, mean arterial pressure, heart rate, carotid pulse pressure, duration of menopause and previous use of hormone replacement therapy, IMT remained significantly lower among tamoxifen users (p<0.00001). The impact of the use of tamoxifen on IMT (-70 µm) could be considered as equivalent to spontaneous evolution with 12 years of aging (+5 µm per year) in this cohort. **Conclusions:** These results suggest that the use of tamoxifen influences significantly the carotid IMT in postmenopausal women. These findings support a vascular protection conferred by SERM which could prevent atherosclerosis.

P0749 CAROTID ARTERY REMODELING AND COMPLETANCE, INSULIN RESISTANCE, AND LIPID METABOLISM IN TYPE 2 DIABETIC PATIENTS

Vittono E, Morizzo C, Kozakova M, Natali A, Toschi E, Baldassarre D, Amato M, Ferrarini R, Palombo C, Departments of Internal Medicine, University of Pisa, CNR Institute of Clinical Physiology, Institute of Pharmacological Sciences, University of Milan, Italy. E-mail: palombo@ifp.cnr.it

Objective: Increased large artery intima-media thickness (IMT) and decreased compliance have been reported in type 2 diabetes mellitus (D). Some features of this insulin resistance syndrome (IRS), such as dyslipidemia and hyperinsulinemia, may play a role in the macrovascular damage of diabetic patients. The aim of our study was to assess the role of IRS and its related metabolic derangements in the remodeling and stiffening of common carotid artery (CCA) in diabetic patients.

Design and Methods: 18 treated diabetic patients (16 males) without clinical evidence of cardiovascular and/or cerebrovascular disease were studied. Age was 61±2 years (mean±SEM), duration of disease 7±1 years, BMI 27.4±0.5 kg/m², HbA1c 6.9±0.3%, and BP 132±17/42±11 mmHg. Insulin sensitivity (IS) was assessed by 2-h euglycemic hyperinsulinemic (40 mU/min/m²) clamp. CCA IMT and cross-sectional diameter were measured by 2D high-resolution US. CCA compliance was determined from simultaneous recording of carotid lumen diameter (Wall Track System 200, Pic Medical) and finger arterial BP, and expressed as area under the compliance BP curve (CCA-AUC) over a standard range of BP (70-130 mmHg).

Results: Insulin-stimulated glucose uptake (M) was 33±3 µmol/min/kg free fatty mass. By using an M value below 2 SD below the mean of our control group, 9 patients were insulin resistant (IR) (25±4 µmol/min/kg) and 9 were insulin sensitive (IS) (45±2 µmol/min/kg). Compared to the IS group, IR patients showed significantly lower CCA-AUC (0.154±0.036 vs 0.091±0.044 mm²/mmHg/100 mg, p<0.02) and higher fasting plasma concentrations of insulin (22.5±2.8 vs 8.8±1.1 mU/ml, p<0.002), and triglycerides (TG: 160±16 vs 60±10 mg/dl, p<0.05). Fasting glucose, HbA1c, BMI, serum cholesterol, age, BP, IMT and CCA diameter were similar between groups. In a univariate analysis, CCA-AUC correlated directly with M (r=0.60, p=0.02) and inversely with TG and insulin (r=-0.59 and -0.71, respectively, p<0.05 for both), whereas IMT correlated inversely with HDL cholesterol (r=-0.51, p<0.05). By multivariate analysis, age, M and TG remained independently associated with CCA-AUC (p=0.004, p=0.004, p=0.004, respectively).

Conclusions: In diabetic patients, insulin resistance is associated with higher stiffness of the common carotid artery. Diabetic dyslipidemia appears to be involved in the functional and structural abnormalities of large arteries.

P0750 CCA STRUCTURE AND FUNCTION OF LARGE ARTERIES IN PATIENTS WITH PSEUDOXANTHOMA ELASTICUM: INCREASED COMPRESSIBILITY OF THE ARTERIAL WALL TO A

Boulayrie P, Zidi M, Carenzi F, Genmain JP, Laloux B, Gacour S, APH Pharmacology Unit, HEGP, Paris, France; Genetica Unit, HEGP, Paris, France; Laboratoire de Mécanique Physique Créteil, France. E-mail: pierre.boulayrie@ggk.ap-hop-paris.fr

Objective: Pseudoxanthoma elasticum (PXE) is a genetic disease characterized by proteoglycan accumulations and imperfect elastogenesis, leading to the late occurrence of large artery calcifications and stenosis. Large artery structure and function has never been described in PXE. Arterial wall is considered as non-compressible since it is required for applying simpler mechanical models. Compressibility of the arterial wall (CAW) has never been studied in vivo in man and the influence of extracellular material on CAW has never been investigated.

Design and Methods: We studied 19 patients with PXE and 15 normal control subjects (Co) matched for age, sex and blood pressure. Common carotid artery and radial artery IMT and diameter were measured with echotracking technique and CAW was assimilated to the average systolic-diastolic % change in WCSA.

Results: Common carotid artery IMT, diameter and stiffness was comparable in PXE and controls. Radial artery diameter was smaller, and distensibility higher than in controls, whereas IMT did not differ. Carotid CAW was 44% higher in patients with PXE than in controls (6.8±1.6% vs 4.7±1.1%, respectively, p<0.05). In control subjects, CAW decreased with age in a linear fashion (r=0.75, p<0.01). In PXE patients, this relationship with age was quadratic (r=0.53, p<0.01), CAW increasing with age before 26, and decreasing sharply thereafter.

Conclusions: Patients with pseudoxanthoma elasticum have a eutrophic inward remodeling of the radial artery, and no geometric change in the carotid artery. Compressibility of the arterial wall is measurable in vivo, non-invasively in humans. The higher CAW in PXE patients suggests that accumulations of proteoglycans and imperfect elastogenesis are important determinants of compressibility.

P0751 ALDOSTERONE TO RENIN RATIO AS A DETERMINANT OF AORTIC STIFFNESS (PULSE WAVE VELOCITY) IN HYPERTENSIVE PATIENTS

Polonia L, Silva LA, Maldonado J. Hypertension & CV Risk Unit, Hospital Pedro Hispano, Matosinhos, Portugal. E-mail: jpolonia@mail.telepac.pt

Objective: Aldosterone to renin ratio (ARR) is an indicator of inappropriate aldosterone activity in hypertension. Since aldosterone may induce vascular fibrosis and contribute to deterioration of vascular compliance, we hypothesized that the ARR could be related to aortic stiffness as measured by carotid-femoral pulse wave velocity.

Design and Methods: Plasma sampling from 60 (32 males) untreated hypertensives (aged 46±2 (SEM) years, body mass index 29±2 kg/m²) were taken for plasma renin activity (PRA, ng/ml/h) and plasma aldosterone (ALD, ng/dl) measurements (by RIA). ARR was calculated by dividing ALD by PRA. Each patient underwent noninvasive measurement of carotid-femoral pulse wave velocity (PWV) m/s with Complior. Linear and multiple correlations between PWV and casual systolic BP (SBP), diastolic BP, DBP and ARR values were assessed.

Results: Values of PWV (10.6±0.3 m/s), SBP (134±3 mmHg), DBP (96±2 mmHg) and of ARR (22.2±2.1) were obtained. ARR was significantly correlated with age (r=0.49, p<0.01), SBP (r=0.44, p<0.01), DBP (r=0.34, p<0.02) and with ARR (r=0.44, p<0.01). In a multiple regression analysis age, casual SBP, casual DBP and ARR emerged as significant (p<0.01) independent predictors of PWV, predicting, respectively (adjusted R squared) 22%, 19%, 11% and 21% of the variation of PWV values.

Conclusions: We conclude that there was an independent and significant correlation between aldosterone to renin ratio and aortic pulse wave velocity, suggesting that in hypertensives inappropriate aldosterone activity may be involved in the increase of aortic stiffness.

P0752 MTEC STUDY (MEDIA INTIMA THICKNESS EVALUATION WITH CANDESARTAN) BASELINE CHARACTERISTICS OF THE FIRST 100 PATIENTS

Barcelo J, Nave D, Garcia S, Mallou J, M. J. Cardiology and Hypertension University Hospital Grenoble, France; Tahade P, France

Design and Methods: MTEC is a randomized double-blind parallel prospective clinical trial. A total of 250 patients without insulin and with HbA1c > 10% will be recruited. To date, 193 patients have been included and 158 randomized by 212 investigators (from 19 French ultrasound centers).

Results: 65.8% male patients have been included in the study, the mean age is 59.5±8.6 years and the mean BMI is 30.8±7.1 kg/m². Hypertension have been diagnosed since 8.0±8.1 years and 63.3% of them have an antihypertensive treatment. The lipid parameters are as follows: triglycerides 1.57±0.84 g/L total cholesterol 2.06±0.39 g/L and LDL cholesterol 1.2±0.32 g/L. The mean blood pressure values are 151.6±11.6 mmHg for SBP, 91.9±7.5 mmHg for DBP and 63.8±11.8 mmHg for pulse pressure. The initial dosage is doubled in 56.3% of patients and 26.8% added hydrochlorothiazide 12.5 mg. The patients have a type 2 diabetes since 6.9±6.9 years with a mean value of HbA1c of 7.15±1.39%, 84.2% of them are treated with an antidiabetic drug. The mean carotid IMT calculated by ultrasonography is 0.76±0.15 mm for right carotid and 0.78±0.15 mm for left carotid.

W
E
B
S
T
E
R
S